CLAIMS

What we claim is:

1. A composition for delivering a 5-HT_3 antagonist across the oral mucosa comprising:

at least one 5-HT_3 antagonist, wherein the 5-HT_3 antagonist is at least partly in an ionized form, the ionized form capable of being converted into an un-ionized form; and

a buffer system,

wherein the buffer system comprises at least two different buffering agents and is capable of changing the pH of saliva from an arbitrary initial pH to a predetermined final pH, independent of the arbitrary initial pH, and of sustaining the predetermined final pH for a period of time, and

wherein the predetermined final pH favors substantially complete conversion of the ionized form to the un-ionized form.

2. The composition of claim 1 wherein the predetermined final pH is within a range of from about 7.1 to about 11.5.

3. The composition of claim 2 wherein the predetermined final pH is within a range of from about 9 to about 11.

4. The composition of claim 1, wherein the composition is formulated as a lozenge, a chewing gum, or a dissolving tablet.

5. The composition of claim 4 formulated as a lozenge.

6. The composition of claim 4 formulated as a dissolving tablet.

7. The composition of claim 4 formulated as a chewing gum.

8. The composition of claim 1 further comprising a gum base.

9. The composition of claim 8 wherein the gum base comprises at least one hydrophobic polymer and at least one hydrophilic polymer.

10. The composition of claim 8, wherein the at least one hydrophilic polymer and the at least one hydrophobic polymer are independently selected from the group consisting of a natural polymer, a synthetic polymer, and mixtures thereof.

11. The composition of claim 10, wherein the at least one hydrophobic polymer is selected from the group consisting of a butadiene-styrene copolymer, butyl rubber, polyethylene, polyisobutylene, polyvinyl acetate phthalate, and mixtures thereof.

12. The composition of claim 11 wherein the hydrophobic polymer comprises a mixture of butyl rubber and polyisobutylene.

13. The composition of claim 1 wherein the predetermined final pH favors at least 80% conversion of the ionized form to the un-ionized form.

14. The composition of claim 13 wherein the 80% conversion occurs in 10 minutes or less.

15. The composition of claim 1 wherein the predetermined final pH favors at least 95% conversion of the ionized form to the un-ionized form.

16. The composition of claim 15 wherein the 95% conversion occurs in 10 minutes or less.

17. The composition of claim 1 wherein the predetermined final pH favors at least 99% conversion of the ionized form into the un-ionized form.

18. The composition of claim 17 wherein the 99% conversion occurs in 10 minutes or less.

19. The composition of claim 1 wherein the buffering agents are selected from the group consisting of a mixture of a weak acid and the salt of the weak acid, and a mixture of a first base and a second base, the second base being weaker than the first base.

20. The composition of claim 19 wherein the mixture of the first base and the second base are selected from the group consisting of sodium carbonate and sodium bicarbonate, potassium carbonate and potassium bicarbonate, and magnesium carbonate and magnesium bicarbonate.

21. The composition of claim 19 wherein the mixture of the weak acid and the salt of the weak acid is acetic acid and sodium acetate.

22. The composition of claim 20 wherein one buffering agent is sodium bicarbonate and one buffering agent is sodium carbonate.

23. The composition of claim 20 wherein one buffering agent is potassium bicarbonate and one buffering agent is potassium carbonate.

24. The composition of claim 19 wherein the buffering agents are in a weight ratio of from about 2:1 to 1:2.

25. The composition of claim 19 wherein the buffering agents are in a weight ratio of from about 3:1 to 1:3.

26. The composition of claim 19 wherein the buffering agents are in a weight ratio of from about 5:1 to 1:5.

27. The composition of claim 19 wherein the buffering agents are in a weight ratio of from about 10:1 to 1:10.

28. The composition of claim 19 wherein the buffering agents are in a 1:1 ratio by weight.

29. The composition of claim 1 wherein the period of time is at least 5 minutes.

30. The composition of claim 1 wherein the period of time is at least 10 minutes.

31. The composition of claim 1 wherein the period of time is at least 20 minutes.

32. The composition of claim 1 further comprising a penetration enhancer.

33. The composition of claim 1 wherein the 5-HT_3 antagonist is selected from the group consisting of ondansetron, palonosetron, tropisetron, lerisetron, alosetron, granisetron, dolasetron, bernesetron, ramosetron, azaseteron, itasetron, zacopride, and cilasentron.

34. The composition of claim 33 wherein the 5-HT_3 antagonist is ondansetron.

35. The composition of claim 34 wherein the ondansetron achieves a C_{max}/T_{max} within a range of about 0.15 ng/ml x min to about 0.6 ng/ml x min.

36. The composition of claim 35 wherein the ondansetron achieves a C_{max}/T_{max} within a range of about 0.4 ng/ml x min to about 0.6ng/ml x min.

37. The composition of claim 34 wherein the membrane permeability of ondansetron is in the range of about 0.3 cm/s to about 3.25 cm/s.

38. A dissolving tablet for delivering a 5-HT_3 antagonist across the oral mucosa comprising:

a 5-HT_3 antagonist, wherein the 5-HT_3 antagonist is at least partly in an ionized form, the ionized form capable of being converted into an un-ionized form;

a protecting agent, wherein the protecting agent coats at least a portion of the 5-HT_3 antagonist; and

a buffer system,

wherein the buffer system comprises at least two different buffering agents and is capable of changing the pH of saliva from an arbitrary initial pH to a predetermined final pH, independent of the arbitrary initial pH, and of sustaining the predetermined final pH for a period of time, and

wherein the predetermined final pH favors substantially complete conversion of the ionized form to the un-ionized form.

39. The dissolving tablet of claim 38 further comprising a compound selected from the group consisting of a binder, a filler, a flavoring agent, a scenting agent, a coloring agent, a preservative, a plasticizer, a penetration enhancer, an elastomeric solvent, and mixtures thereof.

40. The dissolving tablet of claim 38 wherein the buffering agents are selected from the group consisting of a mixture of a weak acid and a salt of the weak acid, and a mixture of a first base and a second base, the second base being weaker than the first base.

41. The dissolving tablet of claim 40 wherein the mixture of the first base and the second base are selected from the group consisting of sodium carbonate and sodium bicarbonate, potassium carbonate and potassium bicarbonate, and magnesium carbonate and magnesium bicarbonate.

42. The dissolving tablet of claim 40 wherein the mixture of the weak acid and the salt of the weak acid is acetic acid and sodium acetate.

43. The dissolving tablet of claim 41 where one buffering agent is sodium bicarbonate and one buffering agent is sodium carbonate.

44. The dissolving tablet of claim 41 where one buffering agent is potassium bicarbonate and one buffering agent is potassium carbonate.

45. The dissolving tablet of claim 40 wherein the buffering agents are in a weight ratio of from about 2:1 to 1:2.

46. The dissolving tablet of claim 40 wherein the buffering agents are in a weight ratio of from about 3:1 to 1:3.

47. The dissolving tablet of claim 40 wherein the buffering agents are in a weight ratio of from about 5:1 to 1:5.

48. The dissolving tablet of claim 40 wherein the buffering agents are in a weight ratio of from about 10:1 to 1:10.

49. The dissolving tablet of claim 40 wherein the buffering agents are in a 1 to 1 ratio by weight.

50. The dissolving tablet of claim 38 wherein the 5-HT_3 antagonist is selected from the group consisting of ondansetron, palonosetron, tropisetron, lerisetron, alosetron, granisetron, dolasetron, bernesetron, ramosetron, azaseteron, itasetron, zacopride, and cilasentron.

51. The dissolving tablet of claim 50 wherein the 5-HT_3 antagonist is ondansetron.

52. A composition for delivering a 5-HT_3 antagonist across the oral mucosa comprising:

a 5-HT_3 antagonist, wherein the 5-HT_3 antagonist is at least partly in an un-ionized form, the un-ionized form capable of being converted into an ionized form at the normal salival pH; and

a buffer system,

wherein the buffer system comprises at least one buffering agent, and wherein the buffer system is capable of providing an adjusted salival pH such that the 5-HT_3 antagonist remains in its un-ionized form.

53. The composition of claim 52 wherein the buffer system is capable of maintaining the adjusted salival pH for a predetermined period of time.

54. The composition of claim 52 wherein the predetermined period of time is within the range of 5 to 10 minutes.

55. The composition of claim 52, wherein the composition is formulated as a lozenge, a chewing gum, or a dissolving tablet.

56. The composition of claim 55 formulated as a lozenge.

57. The composition of claim 55 formulated as a dissolving tablet.

58. The composition of claim 55 formulated as a chewing gum.

59. The composition of claim 52, wherein the buffer system comprises at least two different buffering agents.

60. The composition of claim 59 wherein the buffering agents are selected from the group consisting of a mixture of a weak acid and a salt of the weak acid, and a mixture of a first base and a second base, the second base being weaker than the first base.

61. A method for treating nausea comprising the steps of:

delivering a therapeutically effective amount of a 5-HT_3 antagonist across the oral mucosa.

62. The method of claim 61 wherein the step of delivering a therapeutically effective amount of a 5-HT_3 antagonist across the oral mucosa comprises the step of providing a composition comprising a 5-HT_3 antagonist and a buffer system

wherein the 5-HT_3 antagonist is at least partly in an un-ionized form, the un-ionized form capable of being converted into an ionized form at the normal salival pH, and

wherein the buffer system comprises at least one buffering agent, and wherein the buffer system is capable of providing an adjusted salival pH such that the 5-HT_3 antagonist remains in its un-ionized form.

63. The method of claim 61 wherein the step of delivering a therapeutically effective amount of a 5-HT_3 antagonist across the oral mucosa comprises the step of providing a composition comprising a 5-HT_3 antagonist, a protecting agent, and a buffer system

wherein the 5-HT_3 antagonist is at least partly in an ionized form, the ionized form capable of being converted into an un-ionized form,

wherein the protecting agent coats at least a portion of the 5-HT_3 antagonist, and

wherein the buffer system comprises at least two different buffering agents and is capable of changing the pH of saliva from an arbitrary initial pH to a predetermined final pH, independent of the arbitrary initial pH, and of sustaining the predetermined final pH for a period of time, and

wherein the predetermined final pH favors substantially complete conversion of the ionized form to the un-ionized form.

64. The method of claim 61 wherein the 5-HT_3 antagonist is selected from the group consisting of ondansetron, palonosetron, tropisetron, lerisetron, alosetron, granisetron, dolasetron, bernesetron, ramosetron, azaseteron, itasetron, zacopride, and cilasentron.

65. The method of claim 64 wherein the 5-HT_3 antagonist is ondansetron.